REMARKS

The Office Action mailed August 12, 2004, has been received and reviewed. Claims 1 through 18 were noted as pending in the Office Action. Claims 3 through 17 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 2 and 18 stand rejected. Applicant has amended claims 1, 2 and 18, and added new claims 19 and 20. Support for the new claims may be found at paragraph [0009] of the as-filed application. Reconsideration of the application as amended herein is respectfully requested.

Confirmation of Election

Affirmation of the provisional election of Group I claims 1, 2 and 18 was required in the Office Action. Applicant hereby confirms the election of Group 1 without traverse.

Priority

Applicant notes the acknowledgement of the claim for foreign priority and is obtaining a certified copy of the EP01200353.9 application, which will be provided to the Office.

35 U.S.C. § 101 Rejections

Claims 1, 2 and 18 were rejected in the Office Action as assertedly directed to non-statutory subject matter under 35 U.S.C. § 101. The Office Action states that these claims "as written, do not sufficiently distinguish over mammalian glyoxalase I enzymes as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products." (Office Action at page 5).

As amended, claim 1 is directed to: "An **isolated** biologically active human phosphorylated glyoxalase I." (emphasis added). As the word isolated has been inserted as suggested in the Office Action, it is requested this rejection be withdrawn.

35 U.S.C. § 112 Rejections

Claims 1, 2 and 18 were rejected in the Office Action as assertedly failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph. The Office Action states that the "claims are genus claims that are directed toward any mammalian phosphorylated

glyoxyalase I of any amino acid sequence and structure." (Office Action at page 5). The Office Action states that "the specification fails to provide a written description of additional mammalian glyoxalase I enzymes as encompassed by the claimed genus" although it notes that the "specification discloses a human glyoxalase I" (Office Action at page 6).

As noted previously herein, amended claim 1 is directed to: "An isolated biologically active **human** phosphorylated glyoxalase I." (emphasis added). Amended claim 1 (and dependent amended claim 18) is thus supported by an adequate written description, as noted in the Office Action.

35 U.S.C. § 103(a) Obviousness Rejections

Obviousness Rejection Based on Ranganathan et al. in view of Pestka et al.

Claims 1, 2 and 18 were rejected in the Office Action as assertedly being obvious over Ranganathan et al. (J. Biol. Chem. 1993 Mar. 15; 268(8):5661-7) ("Ranganathan") in view of Pestka et al. (Protein Expr. Purif. 1999 Nov.; 17(2):203-14) ("Pestka").

The Office Action states that claims 1, 2 and 18 differ from the teachings of Ranganathan "only in that the human glyoxalase I taught by Ranganathan et al. is not phosphorylated." (Office Action at page 7). The Office Action goes on to state that it would have been obvious "to phosphorylate the human glyoxalase I as taught by Ranganathan et al using the methods for phosphorylating proteins taught by Pestka et al." and that "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to do this so that the phosphorylated human glyoxalase I can then be used in a wide variety of applications as taught by Pestka et al. ... and that introduction of a kinase recognition site allows proteins to keep their essential structure intact." (Office Action at page 7).

At column 2 of page 5663, Ranganathan states that:

> At least four possible phosphorylation sites (2 serine, 2 threonine) can be identified on the human glyoxalase-I sequence (residues 108-111), however, only one is conserved from the bacterial enzyme (residues 99-102). **There have been no reports of phosphorylation of this enzyme and the fact that no such sites exist is no indication that phosphorylation occurs.** (emphasis added).

Applicant respectfully submits that it is well known to those of ordinary skill in the art that phosphorylation of a biologically active unphosphorylated protein often leads to inactivation of the protein. Thus, from the cited references, one of ordinary skill in the art would not be led to expect that phosphorylation of glyoxalase would lead to the biologically active form. Accordingly, the references do not provide a motivation to combine, as suggested in the Office Action, as the expected result would not be useful for such studies.

This conclusion is further bolstered by examination of Ranganathan, which states, at column 1, page 5663, that:

> Some understanding of the catalytic mechanism may be forthcoming from the observation of a 77% identity in the domain matching residues 99-143 of the human protein with 90-134 of the prokaryotic. A plot of the secondary structure of there proteins (fig. 6) also confirms this and indicates that this region of the protein may be important for the activity of the enzyme. (emphasis added).

Ranganathan thus notes that this region (residues 99-143) of the human protein is important for enzyme activity. As noted above, Ranganathan identified at least four possible phosphorylation sites on the human glyoxalase-I sequence (residues 108-111). As these potential sites are within the area identified as important for enzyme activity, phosphorylation thereof, as suggested in the Office Action, would be likely to alter the secondary structure of the protein in this important area. Thus, one of ordinary skill in the art would further not be led to expect that phosphorylation of glyoxalase would lead to a biologically active form and, thus, would not be motivated to do so.

Further, insertion of a kinase recognition site into a human glyoxalase I would add additional amino acid residues to the glyoxalase. This would change the sequence and potentially alter the secondary structure, even before the phosphorylation suggested in the Office Action occurred. Accordingly, one of ordinary skill in the art would even further expect that modifying the glyoxalase, as suggested in the Office Action would result in a biologically inactive form.

As one of ordinary skill in the art would not be motivated to modify the protein as suggested in the Office Action, based on the cited references, it is requested this rejection be withdrawn and the claims allowed.

CONCLUSION

All pending claims are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact applicant's undersigned attorney.

Respectfully submitted,

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